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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,560	06/17/2005	Toshifumi Yamaki	1034232-000033	3894

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
09/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/539,560	YAMAKI ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,23-27,35-39 and 50-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-9,23-27,35-39 and 50-101* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1-9, 23-27, 35-39, 50-101 are pending.

Applicant's preliminary amendments filed on 6/17/2005, 12/27/2005, and 7/18/2007 are acknowledged.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Groups A_1-A_{245745}, claim(s) 2-3, 55, 72, 77-81, 84, drawn in part to a nitrile hydratase which comprises a variant of the α subunit of SEQ ID NO: 1, and a method of use of said nitrile hydratase for producing an amide compound. See below for discussion of scope for these groups.

Groups B_1-B_{507873}, claim(s) 8-9, 55, 72, 77-81, 84, drawn in part to a nitrile hydratase which comprises a variant of the β subunit of SEQ ID NO: 2, and a method of use of said nitrile hydratase for producing an amide compound. See below for discussion of scope for these groups.

Groups C_1-$C_{124807250385}$, claim(s) 2-3, 4-6, 8-9, 55, 72, 77-81, 82-83, 84 drawn in part to a nitrile hydratase which comprises variants of the α and β subunits of SEQ ID NO: 1 and 2, respectively, and a method of use of said nitrile hydratase for producing an amide compound. See below for discussion of scope for these groups.

Groups D_1-D_{245745}, claim(s) 23-24, 25, 26-27, 37, 50-54, 73-76, 85, 89, 99-101, drawn in part to a polynucleotide encoding a nitrile hydratase which comprises a variant of the α subunit of SEQ ID NO: 1, plasmids comprising said polynucleotide, a host cell comprising said polynucleotide, and a recombinant method to make the nitrile hydratase. See below for discussion of scope for these groups.

Groups E_1-E_{507873}, claim(s) 25, 35-39, 50-54, 73-76, 92, 96, 99-101, drawn in part to a polynucleotide encoding a nitrile hydratase which comprises a variant of the β subunit of SEQ ID NO: 2, plasmids comprising said polynucleotide, a host cell comprising said polynucleotide,

and a recombinant method to make the nitrile hydratase. See below for discussion of scope for these groups.

Groups F_1-$F_{124807250385}$, claim(s) 25, 50-54, 73-76, 86-88, 90-91, 93-95, 97-101, drawn in part to a polynucleotide encoding a nitrile hydratase which comprises a variant of the α subunit of SEQ ID NO: 1 and a variant of the β subunit of SEQ ID NO: 2, plasmids comprising said polynucleotide, a host cell comprising said polynucleotide, and a recombinant method to make the nitrile hydratase. See below for discussion of scope for these groups.

Group G, claim(s) 56-57, 63-65, 66, 67-71, drawn to a method for modifying an enzyme having nitrile hydratase activity wherein one or more properties are changed, wherein said method requires aligning the amino acid sequence of a nitrile hydratase with the sequences of SEQ ID NO: 98/99, identifying specific amino acid residues, and performing modifications at these specific amino acid residues

Group H, claim(s) 58, 63-65, 67-71, drawn to a method for modifying an enzyme having nitrile hydratase activity wherein one or more properties are changed, wherein said method requires inferring the stereostructure of the nitrile hydratase before modification by carrying out an alignment based on the nitrile hydratase stereostructure and the amino acid sequence of PDB ID NO: 1IRE, and wherein said method requires specifying the amino acid residues of specific helices.

Group I, claim(s) 59, 61, 62, 63-65, 67-71, drawn to a method for modifying an enzyme having nitrile hydratase activity wherein one or more properties are changed, wherein said method requires inferring the stereostructure of the nitrile hydratase before modification by carrying out an alignment based on the nitrile hydratase stereostructure and the amino acid sequence of PDB ID NO: 1IRE, and wherein said method requires specifying specific amino acid residues.

Group J, claim(s) 60, 63-65, 67-71, drawn to a method for modifying an enzyme having nitrile hydratase activity wherein one or more properties are changed, wherein said method requires inferring the stereostructure of the nitrile hydratase before modification by carrying out an alignment based on the nitrile hydratase stereostructure and the amino acid sequence of PDB ID NO: 1IRE, and wherein said method requires specifying the region which forms a cavity through which a substrate passes from the outside of the enzyme toward the active center, or vice versa.

2. The inventions listed as Groups A-J do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

3. According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding special technical feature is a contribution over the prior art. The inventions listed as Groups A-J do not relate to a single general inventive concept because they lack the same or

corresponding special technical feature. The technical feature linking groups A-J is a nitrile hydratase which is shown by Kobayashi et al. (Biochimica et Biophysica Acta 1129:23-33, 1991; cited in the IDS) to lack novelty or inventive step since Kobayashi et al. teach a nitrile hydratase comprising an α and β subunit wherein the α subunit of said nitrile hydratase comprises amino acid substitutions at positions 37th (Thr to Val), 71st (Arg to Thr), and 148th (Gly to Glu) of SEQ ID NO: 1. It is noted that the nitrile hydratase of claim 1 is not limited with regard to the number of amino acid substitutions/modifications that can be made. Therefore, any nitrile hydratase having additional modifications/substitutions would meet the recited limitations as long as the substitutions at the recited positions are present. The α subunit of the nitrile hydratase of Kobayashi et al., while also having other modifications compared to the α subunit of SEQ ID NO: 1, is a variant of the α subunit of SEQ ID NO: 1 which has substitutions at the recited positions. Thus, the technical feature does not make a contribution over the prior art and the claimed inventions do not meet the requirement of unity of invention under PCT Rule 13.2.

4. According to PCT Rule 13.2 unity of invention exist only when there is a shared same or corresponding special technical feature among the claimed inventions. The proteins of Groups A-C, the polynucleotides of Groups D-F, and the methods of Group G-J lack a shared same or corresponding special technical feature since the technical feature of Groups A-C is a protein, the technical feature of Groups D-F is a nucleic acid, and the methods of Groups G-J is a method of modifying any nitrile hydratase. The proteins of Groups A-C and the nucleic acids of Groups D-F are not required to be made by the methods of Groups G-J and can be made by other methods or isolated from nature. The methods of Groups G-J while being methods for modifying an enzyme having nitrile hydratase activity, require different steps. Each of the proteins of Groups A-C have different structures (amino acid sequences) whereas each of the nucleic acids of Groups D-F have different structures (nucleotide sequences). Thus, none of the special technical features is shared by or corresponds to any of the inventions of Groups A-J.

5. Groups A-F as written above encompass an extremely large number of protein/nucleic acid variants. Groups A_1-A_{245745} and D_1-D_{245745} encompass at least 245745 variants based on the positions recited in claims 1-2, 23-24 which can be modified (245760 = $(2^{14}-1)x(2^4-1)$; 14 = number of positions in claims 2, 24; 4 = number of positions in claims 1, 23). Groups B_1-B_{507873} and E_1-E_{507873} encompass at least 507873 variants based on the positions recited in claims 7-8, 35-36 (507873 = $(2^{14}-1)x(2^5-1)$; 14 = number of positions in claims 7, 35; 5 = number of positions in claims 8, 36). Groups C_1-$C_{124807250385}$ and F_1-$F_{124807250385}$ encompass at least 124807250385 variants based on the positions recited in the claims 1-2, 4-5, 7-8, 23-24, 35-36, 82-83, 86-87, 93-94 (124807250385 = $(2^{14}-1)x(2^4-1)x(2^5-1)x(2^{14}-1)$; 14 = number of positions in claims 2, 24, 83, 94; 14 = number of positions in claims 4, 35, 86; 4 = number of positions in claims 1, 23, 82, 93; 5 = number of positions in claims 5, 36, 87). In view of the extremely large number of variants encompassed by the groups, the Examiner has not been able to indicate the specific variant that corresponds to each of the groups indicated above (e.g., Group A_x is directed to a nitrile hydratase which comprises a variant of the α subunit of SEQ ID NO: 1, wherein said variant has a substitution at position 36th of SEQ ID NO: 1, Group A_y is directed to a nitrile hydratase which comprises a variant of the α subunit of SEQ ID NO: 1, wherein said variant has a substitution at positions 36th and 71st of SEQ ID NO: 1, Group A_z is directed to a nitrile hydratase which comprises a variant of the α subunit of SEQ ID NO: 1, wherein said variant has a substitution at positions 36th , 71st and 203rd of SEQ ID NO: 1, etc.). Therefore, if any of Groups A-F is elected, Applicant is requested to further indicate a single protein/nucleic acid variant for examination on the merits by providing the specific positions where the modifications are present (e.g., Group C, nitrile hydratase which comprises a variant of the α subunit of SEQ ID NO: 1 and a variant of the β subunit of SEQ ID NO: 2, wherein said α subunit variant has a substitution at positions 36th , 71st and 203rd of SEQ ID NO: 1, and wherein said β subunit variant has a substitution at position 10th of SEQ ID NO: 2). This is not an election of species. The variants lack unity of invention for the reasons already discussed above.

6. Claim 1 link(s) inventions A and C. Claim 7 link(s) inventions B and C. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 1 and 7. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104. Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

7. The Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

8. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims

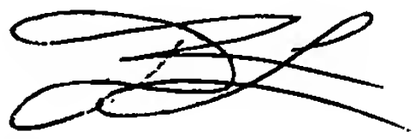
to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

9. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention. The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention. Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



Delia M. Ramirez, Ph.D.
Primary Patent Examiner
Art Unit 1652

DR
September 18, 2007